New treatments for psychotic disorders

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In *The Lancet Psychiatry*, Daniel Freeman and colleagues[1] report the results from their trial that investigated the clinical effects of an intervention targeting worry in patients with non-affective psychosis. The authors accurately write in their Introduction that treatments for psychotic conditions, such as schizophrenia, need substantial improvement. The first-line treatment of schizophrenia—ie, antipsychotics—can suppress delusions and hallucinations, but patients still suffer from other symptoms such as negative symptoms, and often report adverse side-effects from the medication (eg, apathy, neurological side-effects, serious weight gain, and sexual dysfunction). The percentage of non-compliance with medication in patients with schizophrenia is as high as 40–50%,[2] and 74% of patients discontinue their medication within 18 months.[3] Furthermore, Wunderink and colleagues[4] report that dose reduction or discontinuation of antipsychotics during the early stages of remitted first-episode psychosis is associated with superior long-term (7 years) recovery rates (40·4%) compared with the rates achieved with antipsychotic maintenance treatment (17·6%). Additionally, Morrison and colleagues[5] reported that cognitive therapy significantly reduced psychiatric symptoms and seems to be a safe and acceptable alternative for people with schizophrenia and related disorders who have chosen not to take antipsychotic medication. In consideration of low patient compliance with antipsychotics,[2,3] evidence for improved long-term functional recovery with dose reduction or discontinuation of antipsychotic medication,[4] and the promising results from trials of psychological treatments,[5] intervention options for patients with a psychotic disorder are clearly needed that are effective, have fewer side-effects, and are more acceptable to some patients than antipsychotics.

Freeman and colleagues[1] show in their randomised controlled trial of 150 patients with persecutory delusions that a six session, worry-reduction cognitive behaviour therapy (CBT) intervention added to standard care led to significant reductions in both worry (mean difference 6·35 [SE 1·56] Penn State Worry Questionnaire units, 95% CI 3·30–9·40; p<0·001) and persecutory delusions (mean difference 2·08 [SE 0·73] Psychotic Symptoms Rating Scale units, 95% CI 0·64–3·51; p=0·005) compared with standard care alone. The intervention aimed to reduce time worrying and did not directly target the delusions themselves. In addition to significant reductions in worry and persecutory delusions, the intervention also led to significant improvements in overall psychiatric symptoms, paranoid thinking, psychological wellbeing, and rumination. Furthermore, the results of a mediation analysis were consistent with a causal role for worry in paranoia (ie, the change in worry accounted for 66% of the change in delusion).

A few important questions about this study need to be addressed in future research. First, can the worry CBT intervention in combination with modular interventions targeting other key causal factors, such as sleep disturbance and low self-esteem, reduce the dose of antipsychotics needed for patients with psychotic disorders? Second, do these modular interventions improve outcome for patients with an At Risk Mental State (ARMS) for developing a first psychosis[6] when they are added to a more comprehensive CBT? A CBT developed especially for ARMS patients that targets the effects of cognitive biases, such as jumping to conclusions, and encompassing psychoeducation about prepsychotic symptoms, has been shown to reduce the chance of transition to a first psychosis by about 50%.[7,8] The first treatment option for ARMS patients should be CBT because there is cumulative evidence that this type of intervention is effective and without adverse effects in this patient group,[9] and international treatment guidelines advise against treating ARMS patients with antipsychotics.[10] In ARMS patients, worrying, sleep disturbances, negative effects of reasoning biases, and low self-esteem often have an important role in the onset, maintenance, and exacerbation of psychotic symptoms. Targeting these factors with optional modules that are incorporated in a more comprehensive CBT could further improve prognosis in ARMS patients. Intervention in the prepsychotic phase is more effective than intervention during a first psychotic episode because patients are in a more treatment-responsive stage of illness, in which psychosocial and neurobiological damage is less extensive. Clinical experience and research

results show that a patient can be more easily engaged in treatment if distress is prominent while illness-insight is still largely intact, leading to better treatment outcomes.

In conclusion, the study by Freeman and colleagues[1] is an important contribution that fits with the current movement towards evidence-based, benign treatment options for patients with a psychosis spectrum disorder. Furthermore, the study fits with the trend towards transdiagnostic interventions in psychiatry. Cumulative evidence suggests that the DSM categories for mental disorders might not be valid, both from a biological and a clinical perspective.[11] Worrying occurs in many psychiatric disorders, both in the ARMS phase and in later stages, and targeting worry could lead to improved outcomes, irrespective of DSM diagnosis. Freeman and colleagues' study[1] has important implications for clinical practice and research, and I hope their treatment manual will be widely disseminated soon.

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I declare no competing interests.

1 Freeman D, Dunn G, Startup H, et al. Effects of cognitive behaviour therapy for worry on persecutory delusions in patients with psychosis (WIT): a parallel, single-blind, randomised controlled trial with a mediation analysis. *Lancet Psychiatry* 2015; published online March 4. http://dx.doi.org/10.1016/S2215-0366(15)00039-5.
2 Lacro JP, Dunn LB, Dolder CR, et al. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *J Clin Psychiatry* 2002; **63:** 892–909.
3 Lieberman JA, Stroup TS, McEvoy JP, et al, and the CATIE investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005; **353:** 1209–23.
4 Wunderink L, Nieboer RM, Wiersma D, et al. Recovery in remitted first-episode psychosis at 7 years of follow-up of an early dose reduction/discontinuation or maintenance treatment strategy: long-term follow-up of a 2-year randomized clinical trial. *JAMA Psychiatry* 2013; **70:** 913–20.
5 Morrison AP, Turkington D, Pyle M, et al. Cognitive therapy for people with schizophrenia spectrum disorders not taking antipsychotic drugs: a single-blind randomised controlled trial. *Lancet* 2014; **383:** 1395–403.
6 McGorry PD, Yung AR, Phillips LJ. The "close-in" or ultra high-risk model: a safe and effective strategy for research and clinical intervention in prepsychotic mental disorder. *Schizophr Bull* 2003; **29:** 771–90.
7 Van der Gaag M, Nieman DH, Rietdijk J, et al. Cognitive behavioural therapy for subjects at ultra high risk for developing psychosis: A randomized controlled clinical trial. *Schizophr Bulletin* 2012; **38:** 1180–88.
8 Van der Gaag M, Nieman DH, Van den Berg D. CBT for those at risk for a first episode psychosis: evidence based psychotherapy for people with an 'at risk mental state'. Oxford: Routledge, 2013.
9 Hutton P, Taylor PJ. Cognitive behavioural therapy for psychosis prevention: a systematic review and meta-analysis. *Psychol Med* 2014; **44:** 449–68.
10 International early psychosis association writing group. International clinical practice guidelines for early psychosis. *Br J Psychiatry* 2005; **187:** S120–24.
11 Insel T, Cuthbert B, Garvey M, et al. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. *Am J Psychiatry* 2010; **167:** 748–51.

Diagnosis of dependence to prescribed pain medication

In *The Lancet Psychiatry*, Louisa Degenhardt and colleagues[1] aim to establish how definitions of opioid use disorder or dependence in WHO's ICD-10 and ICD–11[2] and the American Psychiatric Association's DSM-IV and DSM-5[3] classified individuals in POINT, an Australian community sample of people prescribed pharmaceutical opioids for chronic non-cancer pain.

This study is both relevant and important for public health care due to increasing rates of long-term prescribing of opioids for chronic pain in many high-income countries, particularly the USA, Australia, and Canada,[4,5] and growing concern about the associated increases in problematic use of and dependence to these opioids.[6,7] Accurate diagnosis of dependence and disorder in this group is needed to target treatment effectively. Moreover, DSM-5 was released in 2013[3] and the ICD system is currently undergoing revision, and so it is timely to examine these classification systems.[2]

The study by Degenhardt and colleagues[1] provides empirical evidence for how different diagnostic criteria for opioid dependence or disorder classified individuals receiving opioids for pain. Sampling 1422 people who had been taking strong opioids for their pain for a median of 4 years (IQR 1·5–10·0), the authors reported that 8·5–9·9% of participants met lifetime criteria for dependence when they used DSM-IV, ICD-10, and ICD-11. 20·8% of participants fit criteria for use disorder in DSM-5 (when restrictions were applied). DSM-5 differs from other classifications by using a single category in which dependence and problematic use are measured on a continuum (mild, moderate, and severe use disorder) and in which physiological responses of tolerance and withdrawal are excluded if the patient is being prescribed opioids for chronic pain and adheres to their prescription. When tolerance and withdrawal were included, irrespective of the patient's adherence,


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